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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,504	09/26/2003	Steven Leigh	032553-037	8609

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

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08/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,504	LEIGH ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 6-8-07 is acknowledged.

Claims included in the prosecution are 23-42.

In view of the amendments, the 112, the 102 rejections over WO 00/16770, Weder and 103(a) rejection over Watts et al or Weder further in view of Leigh (5,004,611) are withdrawn.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 23-30, 32-37 and 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Janoff et al (5,616,334).

Janoff teaches a method of encapsulation of water insoluble drugs such as amphotericin B. The method involves adding the ethanolic solutions of the drug to liposomal suspension in an aqueous medium. The liposomal sizes can vary from sizes of 0.2 microns (col. 5, lines 24-43; col. 15, lines 1-9, Examples 9 and 21). Since the liposomal composition is added with the drug solution or dispersion, the presence these in separate containers is implicit and the reference meets the requirements of instant claims. Various phospholipids are disclosed on col. 8, line 58 through col. 9, line 19. The drug-lipid ratios in example 9 falls within the range claimed in instant claims. The addition of the term,' kit' does not carry any patentable weight since the claims still

recite two containers and the intended use has no significance in composition or kit claims.

3. Claims 23-34, 36-37 and 40-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Watts et al (6,383,513).

Watts et al disclose a composition containing a water insoluble cannabinoid, ethanol, fatty acids, poloxamers and egg yolk phospholipid (which contains both phosphatidylcholine and phosphatidylethanolamine) and a method of preparation (col. 3, lines 35-67). The method involves combining the cannabinoid, ethanol, and fatty acid to aqueous dispersion of phospholipid (Example 6). Since liposomes are formed spontaneously when the phospholipids are hydrated with and aqueous medium, the reference meets the requirements of instant claims. Since the method involves homogenization, in the absence of showing otherwise, the reference meets the requirements of sizes of liposomes in instant claims.

The examiner has already cited the reference of Mehta, which shows that the addition of an aqueous medium to a phospholipid would result in the formation of liposomes (Example 1).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 24, 27-29, 35, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al.

The teachings of Watts et al have been discussed above.

Watts et al do not specifically teach that the hydrophobic agent should be in the form of an amorphous powder. The criticality of the nature of the agent however, is unclear to the examiner since once it is incorporated within the liposomes, the active agent does not exist in a solid form. Watts et al also do not specifically teach the sizes of the liposomes. However, since, the liposomal composition is homogenized, it would have been obvious to one of ordinary skill in the art that they would be of claimed sizes. Sizes of liposomes are also deemed to be obvious parameters manipulated by an artisan to obtain the best possible results. Although Watts et al do not teach sterilization of the composition, since any composition administered to humans, should not be contaminated with microorganisms sterilization is deemed to be a manipulatable step practiced by an artisan.

6. Claims 23-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al in view of Portnoff (5,583,052).

Watts et al as discussed above, disclose a composition containing a water insoluble cannabinoid, ethanol, fatty acids, poloxamers and egg yolk phospholipid (which contains both phosphatidylcholine and phosphatidylethanolamine) and a method of preparation (col. 3, lines 35-67). The method involves combining the cannabinoid, ethanol, and fatty acid to aqueous dispersion of phospholipid (Example 6). Since

liposomes are formed spontaneously when the phospholipids are hydrated with and aqueous medium, the reference meets the requirements of instant claims. What are lacking in Watts are the explicit teachings of two containers for the formulation, a kit and the sterilization of the components.

Portnoff teaches a kit containing two containers. One contains liposomes and the other the active agent. The compositions are sterilized (Example 1). What is lacking in Portnoff are the teachings of the use of instant phospholipids, solvents and other excipients such as fatty acids, poloxamers and a specific teaching that the active agent is a hydrophobic agent.

It would have been obvious to one of ordinary skill in the art to supply the compositions of Watts et al in two containers and in a sterilized kit form with a reasonable expectation of success since Portnoff teaches the art known knowledge of supplying the liposomes and the active agent separately and in sterilized form. Alternately, to use a hydrophobic agent as an active agent and to use fatty acids or poloxamer for the solubilizing the active agent with a reasonable expectation of success since the reference of Watts et al teach the formation of active agent loaded liposomes using the hydrophobic agents, fatty acids and poloxamers.

7. Claims 23-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janoff et al in view of Portnoff (5,583,052).

The teachings of Janoff et al have been discussed above. . What are lacking in Janoff are the explicit teachings of two containers for the formulation, a kit and the sterilization of the components.

The teachings of Portnoff have been discussed above. It would have been obvious to one of ordinary skill in the art to supply the compositions of Janoff et al in two containers and in a sterilized kit form with a reasonable expectation of success since Portnoff teaches the art known knowledge of supplying the liposomes and the active agent separately and in sterilized form.

8. Claims 31 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janoff et al (5,616,334) in combination with Leigh (5,004,611).

Janoff teaches a method of encapsulation of water insoluble drugs such as amphotericin B. The method involves adding the ethanolic solutions of the drug to liposomal suspension in an aqueous medium. The liposomal sizes can vary from sizes of 0.2 microns (col. 5, lines 24-43; col. 15, lines 1-9, Example 9).

What is lacking in Janoff is the inclusion of a surfactant in the ethanolic solution.

Leigh while disclosing liposomal formulations teaches that the inclusion of surfactants such as sorbitans sold as SPANS increases the entrapment efficiency and also strengthens the liposomes in some way (abstract and col. 5, lines 1-12).

The inclusion of a surfactant in the method of loading an active agent taught by Janoff and prepare a composition containing a water insoluble active agent would have been obvious to one of ordinary skill in the art since such an inclusion would increase the entrapment efficiency and also strengthen the liposomes as taught by Leigh.

Applicant's arguments have been fully considered, but are deemed to be moot in view of these new rejections.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK